

12

Docket No. UF-260XC1  
Serial No. 09/997,447Remarks

Claims 6-10 and 19-29 were pending in the subject application. By this Amendment, claim 6 has been amended and claims 30-32 have been added. The undersigned avers that no new matter is introduced by this amendment. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 6-10 and 19-32 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Applicants note that the Interview Summary of August 28, 2003 and Office Action of September 11, 2003 indicate that Applicants suggested that claims 6-10 be examined in this application. Applicants respectfully submit that the conversation held with Examiner Spivack on that date was directed to the apparent delay in the preparation of an Office Action in the matter by the previous Examiner. During the course of this conversation, the undersigned indicated that Applicants wished to pursue claims directed to methods of promoting wound healing should the Patent Office consider the inventions patentably distinct. As indicated in the Office Action of September 11, 2003, the Patent Office has apparently restricted the claimed inventions as being patentably distinct since claims 19-29 stand withdrawn from consideration as being directed to non-elected inventions (37 C.F.R. 1.142(b)). Confirmation of the restriction of the two claimed methods is respectfully requested.

Claims 6-10 have been rejected under judicially created doctrine as being drawn to an improper Markush group. Applicants have amended the claims to correct this issue and respectfully request reconsideration and withdrawal of the rejection.

Applicants note that the Office Action indicates that prior art references previously submitted appear to have been separated from the instant application at the Patent Office. Duplicates of the cited references were provided to the Patent Office on September 15, 2003 and consideration of these references is respectfully requested. Applicants further request that the PTO/SB/08A forms relating to the lost references be initialed and returned to Applicant with the next communication from the Patent Office.

Claims 6-10 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Blake *et al.* (WO 00/10610). The Office Action argues that Blake teach the topical administration of

topiramate as an anti-convulsant therapeutic agent linked to a non-cytotoxic bioreductive moiety (pointing to pages 4-14 and 32 and claims 1, 22, and 23). The Office Action argues that the claimed invention is obvious in view of the teachings of the reference that establish a nexus between wound healing in claim 1 and the administration of topiramate in claims 22 and 23. The Office Action also states that the claims define the invention. Applicants respectfully traverse.

Applicants respectfully submit that the cited reference fails to suggest or teach a method of promoting wound healing comprising the use of topiramate, either alone or conjugated to a non-cytotoxic bioreductive moiety. It is well established in the patent law that prior art references must be considered in the context of what they would teach those skilled in the art (emphasis added). See *In re Boe*, 355 F.2d 961, 965, 148 U.S.P.Q. 507, 510 (CCPA 1966) (all of the disclosures in a reference, including non-preferred embodiments, “must be evaluated for what they fairly teach one of ordinary skill in the art”).

As is clear from the claims of Blake *et al.*, therapeutic agents, such as topiramate, are claimed “for use in the treatment of epilepsy” (see claims 22-23), not for the healing of wounds. There is no teaching or suggestion in the claims or the specification of Blake et al. topiramate is to be topically administered for the promotion of wound healing. Additionally, it respectfully submitted that where the reference addresses or claims medicaments for “use in the healing of wounds or the treatment of fibrotic disorders”, the therapeutic agents are limited to growth factor neutralizing agents or agents specific against only fibrotic growth factors (see claims 2 and 3). Specific examples of such agents are TGF- $\beta$ 1; TGF- $\beta$ 2; PDGF; IFN $\gamma$ ; IL-1; TGF- $\beta$ 3; FGF-1; FGF-2; IL-4; IL-10; betaglycan; inhibitors of: IFN- $\gamma$ , at least one integrin receptor, at least one convertase enzyme, or IL-6; stimulators of: IFN- $\gamma$  or activin and/or inhibin; agents that modulate actin assembly and organization, latency associated peptide; insulin like growth factor II; or compounds that influence the sex hormone system (see claims 4-21). Notably absent from the listing of agents for use in the healing of wounds or the treatment of fibrotic disorders in topiramate.

Turning to the teachings of the specification of Blake et al., specification indicates that “the present invention extends the range of conditions to which the drug conjugates of the aforementioned PCT application may be applied to include the healing of wounds, and the treatment of fibrotic disorders, ulcerative colitis, inflammatory bowel disease, epilepsy, cardiovascular reperfusion injury,

cerebral reperfusion injury, hypertension, cystic fibrosis, psoriasis, para-psoriasis, peptic ulcers, gastric ulcers, duodenal ulcers, diabetic ulcers dementia, oncology and AIDS" (page 4, paragraph 3). The specification then proceeds to provide subsections devoted to these classes of diseases or disorders that include the various therapeutic agents that can be used to treat the specified disease or disorder. As indicated *supra*, the sections pointed to in the Office Action (pages 4-14) are solely directed to the use of therapeutic agents such as TGF- $\beta$ 1; TGF- $\beta$ 2; PDGF; IFN $\gamma$ ; IL-1; TGF- $\beta$ 3; FGF-1; FGF-2; IL-4; IL-10; betaglycan; inhibitors of: IFN- $\gamma$ , at least one integrin receptor, at least one convertase enzyme, or IL-6; stimulators of IFN- $\gamma$  or activin and/or inhibin; agents that modulate actin assembly and organization; latency associated peptide; insulin like growth factor II; or compounds that influence the sex hormone system for use in the healing of wounds. On page 15 of the specification, it is explicitly stated:

### 1.3. Epilepsy

The therapeutic agent for use in the treatment of epilepsy may for example be Phenytoin, Phenobarbitone, Sodium Valporate, Topiramite.  
(misspelling in original)

Applicants respectfully submit that one skilled in the art, based on the claims and teachings of the specification would not, and could not, reasonably infer that the reference teaches or suggests that topiramate was to be used for the healing of wounds as is argued by the Patent Office.

Applicants further submit that there would have been no motivation to use topiramate for use in wound healing because such a pharmacological activity for topiramate does not appear to have been recognized in the art prior to the time of invention. As the Patent Office may be aware, topiramate is indicated for use as an anti-convulsant (anti-epileptic) agent for patients with partial onset seizures. As there is no teaching or suggestion in any prior art of record that one of the benefits of anti-convulsant, such as topiramate, included wound healing, it is respectfully submitted that one skilled in the art would not have been motivated to use an anti-convulsant, such as topiramate, in methods of promoting wound healing. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

15

Docket No. UF-260XC1  
Serial No. 09/997,447

In view of the foregoing remarks and amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



Frank C. Eisenschenk, Ph.D.  
Patent Attorney  
Registration No. 45,332  
Phone No.: 352-375-8100  
Fax No.: 352-372-5800  
Address: Saliwanchik, Lloyd & Saliwanchik  
A Professional Association  
2421 NW 41st Street, Suite A-1  
Gainesville, FL 32606-6669

FCE/mv

Attachment: Amendment Transmittal Letter

AMENDMENT TRANSMITTAL LETTER			ATTORNEY'S DOCKET NO. UF-260XC1
SERIAL NO. 09/997,447	FILING DATE November 30, 2001	EXAMINER Phyllis Spivack	GROUP ART UNIT 1614
INVENTION Treatments for Neurogenetic Disorders, Impulse Control Disorders, and Wound Healing			

## TO THE COMMISSIONER OF PATENTS AND TRADEMARKS:

Transmitted herewith is an amendment in the above-identified application.

- Small entity status of this application under 37 CFR 1.27 has been established by a verified statement previously submitted.
- Applicant claims small entity status.
- A verified statement to establish small entity status under 37 CFR 1.9 and 1.27 is enclosed.
- No additional fee is required.
- The fee has been calculated as shown below:

	(1)	(2)	(3)	SMALL ENTITY	OTHER THAN A SMALL ENTITY
	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NO. PREVIOUSLY PAID FOR	PRESENT EXTRA	
TOTAL	* 19	MINUS	** 20	0	
INDEP.	* 2	MINUS	*** 3	0	
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				0	
				RATE  \$ 9  \$43  \$145  Total addit. fee	OR  \$18  \$86  \$290  Total addit. fee
				ADDITIONAL FEE  \$ 0.00  \$ 0.00  \$ 0.00  \$ 0.00	\$0.00  \$0.00  \$0.00  \$0.00
					OR

\* If the entry in Col. 1 is less than the entry in Col. 2, write "0" in Col. 3.

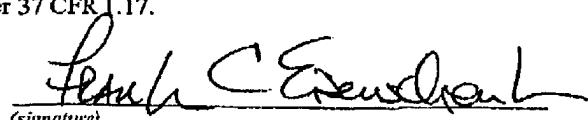
\*\* If the Highest No. Previously Paid For IN THIS SPACE is less than 20, enter "20."

\*\*\* If the Highest No. Previously Paid For IN THIS SPACE is less than 3, enter "3."

The Highest No. Previously Paid For (Total or Indep.) is the highest number found in the appropriate box in Col. 1.

- Please charge my Deposit Account No. 19-0065 in the amount of \$ 0.00.
- A check in the amount of \$ \_\_\_\_\_ to cover the filing fee is enclosed.
- The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 19-0065. Two additional copies of this paper are enclosed.
  - Any additional filing fees required under 37 CFR 1.16.
  - Any patent application processing fees under 37 CFR 1.17.

December 11, 2003  
(date)

  
(signature)